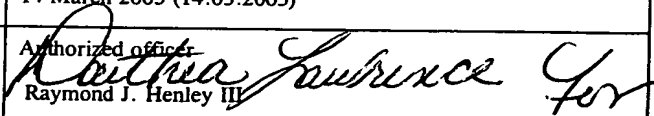


PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 9516-058-228	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US03/36740	International filing date (<i>day/month/year</i>) 17 November 2003 (17.11.2003)	Priority date (<i>day/month/year</i>) 18 November 2002 (18.11.2002)
International Patent Classification (IPC) or national classification and IPC IPC(7): A61K 31/24, 31/40; C07C 205/00; C07D 209/34 and US Cl.: 514/416, 534; 548/512; 560/20		
Applicant CELGENE CORPORATION		
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>4</u> sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of <u> </u> sheets.</p> <p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input checked="" type="checkbox"/> Non-establishment of report with regard to novelty, inventive step and industrial applicability IV <input type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input type="checkbox"/> Certain defects in the international application VIII <input type="checkbox"/> Certain observations on the international application 		
Date of submission of the demand 16 June 2004 (16.06.2004)	Date of completion of this report 14 March 2005 (14.03.2005)	
Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/ US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer  Raymond J. Henley III Telephone No. 571-272-0600	

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International Application No.

PCT/US03/36740

I. Basis of the report

1. With regard to the elements of the international application:*

- ☒ the international application as originally filed.
- ☒ the description:
pages 1-43 as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.
- ☒ the claims:
pages 44-51, as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.
- ☐ the drawings:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.
- ☐ the sequence listing part of the description:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language _____ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages NONE
- ☐ the claims, Nos. NONE
- ☐ the drawings, sheets/fig NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

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III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The question whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

- ☐ the entire international application,
☒ claims Nos. 32

because:

- ☐ the said international application, or the said claim Nos. _____ relate to the following subject matter which does not require international preliminary examination (*specify*):

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _____ are so unclear that no meaningful opinion could be formed (*specify*):

- ☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

- ☒ no international search report has been established for said claims Nos. 32

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the standard.
☐ the computer readable form has not been furnished or does not comply with the standard.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US03/36740

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims <u>1-31 and 33-46</u>	YES
	Claims <u>NONE</u>	NO
Inventive Step (IS)	Claims <u>38-46</u>	YES
	Claims <u>1-31 and 33-37</u>	NO
Industrial Applicability (IA)	Claims <u>1-31 and 33-46</u>	YES
	Claims <u>NONE</u>	NO

2. CITATIONS AND EXPLANATIONS

Claims 1-31 and 33-46 meet the criteria under PCT Article 33(2) for novelty because the prior art fails to teach the presently claimed methods for treating the various diseases and disorder which comprises the administration of the presently claimed enantiomerically pure propionamide or propionate compounds; methods for producing the presently claimed enantiomerically pure propionamide or propionate compounds; or entantiomerically pure propionamde or proprionate compounds.

Claims 1-31 and 33-37 do not meet the criteria under PCT Article 33(3) for inventive step because MULLER (US 5,698,579 A) teaches method of treating the variously claimed diseases/disorders which comprises the administration of racemic mixtures of the presently claimed propionamide compounds.

The difference between the above and the claimed subject matter lies in that MULLER fails to teach the presently claimed enantiomerically pure propionamide compounds.

However, to the skilled artisan, the claimed subject matter would have been obvious because the skilled artisan would have recognized that the activity of a racemic mixture of compounds is the result of the additive effects of the individual isomers. The skilled artisan would have been motivated to select a particular isomer because the artisan would have known that in such racemic mixtures, one isomer is generally more active than the other.

Claims 38-46 meet the criteria under PCT Article 33(3) for inventive step because the prior art fails to teach or suggest the present claimed method for producing the presently claimed enantiomerically pure propionamide or propionate compounds or the entantiomerically pure propionamde or proprionate compounds themselves.

Claims 1-31 and 33-46 meet the criteria under PCT Article 33(4) because the presently claimed methods for treating the various diseases and disorder which comprises the administration of the presently claimed enantiomerically pure propionamide or propionate compounds; methods for producing the presently claimed enantiomerically pure propionamide or propionate compounds; entantiomerically pure propionamde or proprionate compounds themselves would have applicability in the medical industry.